Inquiry into the approval processes for new drugs and novel medical technologies in Australia

Submission from the University of Melbourne

October 2020

The University of Melbourne welcomes to opportunity to provide a submission to the Standing Committee of Health, Aged Care and Sport's Inquiry into the approval processes for new drugs and novel medical technologies in Australia, with a particular focus on those for the treatment of rare diseases and conditions where there is high and unmet clinical need.

The University of Melbourne's research spans all areas of health and medical research, which has led to the discovery of new drugs and treatments. The University's research has also been drawn upon to provide the clinical and health economic evidence to inform decision making which makes these medical advances and treatments available to the Australian public. Importantly, our research extends from addressing the most major and prevalent diseases, to rare diseases and unmet needs of the community.

The University collaborates closely and extensively with medical research institutes and hospitals in the Melbourne Biomedical Precinct and across the world to ensure research is addressing patient and population needs. We partner with industry to successfully translate research towards providing safe and effective drugs, vaccines and treatments. We note the submission from the Melbourne Academic Centre for Health, of which we are a member.

Our comments on the topics outlined in the Terms of Reference are made with the intent to improve translation of research into Australian patient benefits and enhance Australia's position in developing or accessing new drugs and novel medical technologies.

TOR 1. The range of new drugs and emerging novel medical technologies in development in Australia and globally, including areas of innovation where there is an interface between drugs and novel therapies.

The development and eventual adoption of new drugs and innovation depends on evidence-based research that responds to a market/industry need and meets regulatory requirements. To broaden the range of new drugs and emerging novel technologies developed in Australia, in response to Australian patient needs, there needs to be ongoing support for partnerships between researchers, market-leaders and industry to sustain the pipeline of innovation.

Innovations in prostheses (orthopaedic, cardiac, dental) and biomedical devices (implantable and external) are being made at a substantial rate, driven by technology advancements and investment by industry. Australian fundamental research in materials science and electronics, for example, can drive innovations in these products with medical applications. Driving the effort behind medical device advancement and enabling partnership with industry should be a an imperative of government (State and Federal). The mechanisms of funding to support these partnerships (e.g. MTP Connect, MRFF initiatives, CRC-like partnerships between research organisations and industry) should be rationalised to ensure consistency in accessibility, approach and opportunity. Considering new mechanisms, we have previously supported the proposal for a 'collaboration premium' under the R&D Tax Incentive policy that rewards greater industry engagement with research providers. Another potential activity to drive biomedical research translation is that of a so-called 'venture catalyst' such as BioCurate (www.biocurate.com), a joint venture between the State Government, Monash University and the University of Melbourne.

Recommendation 1: Review the current funding mechanisms that facilitate research-industry partnerships in medical device innovation.

Due to ease of measurement, many clinical trials only measure the concentrations of drugs in blood but not in tissue, despite many diseases being tissue specific. Having an understanding of blood pharmacokinetics is necessary but not sufficient for understanding overall drug behaviour and the relationship to cure. Drug optimisation using pharmacokinetics can assist more drugs in clinical trials reach the market for specific indications, particularly with the use of pharmacokinetics to optimise treatments in early phase 2 and 3 trials. Equally, more in-depth evaluation of immunological responses to vaccine candidates could inform optimisation strategies for candidates that in initial studies do not reach required performance measures. This is primarily due to the limited investment available and need for efficient commercial outcomes. As a result, some candidate therapies developed from Australian research can be lost from the pipeline without in-depth analysis.

Recommendation 2: To improve the range of new therapeutics successfully developed in Australia consider mechanisms to support ongoing candidate optimisation and tissue targeting activities. This could be delivered via voucher systems to access specialist capabilities in Universities and Medical Research Institutes.

TOR 2. Incentives to research, develop and commercialise new drugs and novel medical technologies for conditions where there is an unmet need, in particular orphan, personalised drugs and off-patent that could be repurposed and used to treat new conditions.

Repurposed drugs offer huge potential to address existing and emerging unmet needs (such as COVID-19) in a cost and time efficient manner. However, drug repurposing should be based on sound preclinical or clinical evidence and trials should follow the same rigorous design as new drugs in terms of demonstrating efficacy and cost-effectiveness. Given that obtaining intellectual property protection for development or commercial support for off-patent repurposing of drugs for a new indication is very difficult, other sources of funding are needed. Research to evaluate safety and efficacy in drug repurposing therefore requires specific government funding, e.g. via a targeted scheme that would include rigorous evaluation of proposals. Such a program should focus activity on health conditions specifically pertinent to Australia, potentially employing the Global Burden of Disease study as a guide. It is encouraging that the MRFF opened a competitive scheme focusing on Efficient Use of Medicines on the 12th of October 2020 which includes assessment of therapeutic indications for existing medicines that are not currently approved by the TGA.

In addition to accessing funding to demonstrate the utility of repurposed drugs for new indications, it is important to consider the regulatory approval that may be necessary to actually use drugs off-label based on other information, such as genomics for example. Hence a critical platform for support would be a system of national clinical registries. In cancer treatment, every patient considered for off-label use is on a clinical registry with all genomics and clinical data including all previous lines of treatment. Clinical registries in areas of unmet need would support not only the drug repurposing, but also new drugs and novel medical technologies.

Recommendation 3: Enhance programs for translational research on repurposing drugs and the establishment and maintenance of clinical registries.

TOR 3. Measures that could make Australia a more attractive location for clinical trials for new drugs and novel medical technologies.

A barrier to attracting greater clinical trial activity to Australia is the lack of a national approach to multi-site trial recruitment and coordination, and the localised, specialist expertise in more complex, advanced trials for which Australia could be a destination. Initiatives to support national coordination, a framework for site credentialing for specific trial types, and enhanced access to advanced trial design and evaluation expertise would be welcome. The growing adoption of electronic medical records and expansion of digital health initiatives provide opportunities in these areas.

One example for Australia in terms of coordination is the highly efficient and cost-effective centralised model in the UK for multi-centre clinical trials. The UK centralised co-funding model allows simultaneous multicentre trials to be conducted at all hospital sites. Participating hospitals are provided with nurses who recruit for multiple trials. The hospitals are incentivised to participate in trials as they are paid per recruitment of participant, irrespective of who (or where) the principal investigator is based. The advantages of this system include:

- Researchers can establish large multi-centre trials at astonishing speed, drawing on an existing infrastructure (see, for instance, the RECOVERY trial to test successive COVID-19 treatments).
- More questions can be answered, and more drugs evaluated within a short time.
- Smaller provincial hospitals (and rural and remote patients) can be involved in trials, which greatly speeds the pace of discovery.
- The tax dollar is far more efficiently used, compared with funding individual trials and duplicating costs that could be combined.

In addition to improved multi-side coordination, the design and outcomes of trials could be improved through more efficient use of existing and improved capabilities within research-intensive organisations, including Universities, and the NHMRC Advanced Health Research and Translation Centres (such as the Melbourne Academic Centre for Health).

This would support complex trial activity across both public and private hospital sectors as well as the primary care network by providing access to specialised expertise. This would support attraction of clinical trials by enabling a system-wide, high-quality and consistent approach to evaluating new treatments and technologies and would benefit the development of cost-effective models of care.

The R&D Tax Incentive system has been incredibly useful for bringing early phase studies, at least in medical devices, to Australia and also provides significant support to Australian companies in reaching clinical validation of new drugs and novel medical technologies. This system should be strengthened and promoted more vigorously. The impact of cutbacks to the R&D Tax Incentive on clinical trials cannot be understated. Even where clinical trials are considered exempt, proposed changes would impact all companies undertaking early stage research and development and thereby reduce clinical trial activity. As mentioned above, a 'collaboration premium' for industry-research provider engagement may provide further incentive for such engagement.

Recommendation 4: Establish national frameworks that support streamlined multi-centre trial establishment and site-specific credentialing, including the following components:

a) *Establish a harmonised national process for ethical review and authorisation for human trials. This is particularly important for novel types of therapy and particularly in rare diseases.*

b) *Establish a national framework for credentialing of hospitals to participate/lead in trials of new drugs and novel therapies. This would establish clear criteria for undertaking specific types of clinical trials (first-in-human, device trials etc). As part of this framework a national register of credentialled facilities for certain types of trials would be maintained.*

c) *Establish a central coordinating function purposed to promote trials activity, in conjunction with the national register of credentialled facilities.*

Recommendation 5: Establish and support clinical trial hubs that facilitate high quality trial design, prosecution, and analysis and reporting of trial findings, including appropriate health economic assessments.

Recommendation 6: Maintain the R&D Tax Incentive for clinical, pre-clinical research and development for medical devices and therapeutics.

TOR 4. Without compromising the assessment of safety, quality, efficacy or cost-effectiveness, whether the approval process for new drugs and novel medical technologies, could be made more efficient, including through greater use of international approval processes, greater alignment of registration and reimbursement processes or post market assessment.

Post market surveillance mechanisms such as prosthetic registries are often unreliable, requiring years of data collection which is often insufficient in its granularity to provide meaningful interpretation of causes for success or failure. A more pro-active, in-depth interrogation of efficacy, safety and health economic outcomes during the early implementation phase could be undertaken by relevant discipline experts at nationally accredited centres. This would provide a strong evidence base to support broader dissemination (or not) of a new technology. Devices/prostheses are examples of where this is most pertinent as controlled implantation under rigorous scrutiny and subsequent interrogation in specifically credentialed centres is required to truly evaluate cost and clinical effectiveness. Recommendations that support broad adoption of a new treatment should also include recommendations to restrict or prevent existing, less-effective treatment practices where there is strong evidence available. Further discussion is required on the source of such recommendations, which should be independent of funders, driven by the science and healthcare needs, and enabled by a body of experts in clinical care, health economists, and clinical triallists.

Recommendation 7: The creation of nationally accredited centres for early, pro-active assessment of a new innovation's efficacy, safety and health economic outcomes to provide the evidence to support broader dissemination (or not), and disinvestment from existing, ineffective health care practices.

Australia's approval process for new drugs and medical technologies should continue to look to international best practices and innovations with a view to ensuring all Australians can access new therapies wherever an available, high-quality evidence base can support it.

Australian processes should facilitate early dialogue between industry and regulatory agencies to ensure approvals are efficient. Approval processes should support and resource international approaches such as adaptive licensing as promoted by the European Medicines Agency which seeks to support timely access to new therapies where a sufficient evidence base is yet to be established. This is particularly important for rare or neglected diseases, where meaningful trials may be impossible due to the small population, the related costs and time to complete. Equally, approval processes should consider internationally produced evidence of safety and efficacy to support access to proven therapeutics. An example of this issue is the antibiotic Cefiximine that has been shown to be highly effective against gonorrhoea overseas but is not marketed in Australia. To make this available in Australia would require registration in a clinical trial, despite the extensive evidence through it's safe and effective use overseas.

Reimbursement processes in Australia are generally slow, at moments adversarial and often fail to accommodate new technologies. This creates a disconnect between the R&D activities, which broadly are supported and encouraged, and reimbursement support. A mechanism should be established so that early in the development of drugs and devices a collaborative system is developed with MSAC and Medicare that provides much needed security around eventual reimbursement for new drugs and devices. At the moment, particularly with devices, it is an obstacle to investment and a method of providing some level of certainty to this would hasten the development cycle considerably.

We also note the opportunity, driven by COVID-19, to review the PBAC assessment process for publicly funded vaccines. The current assessment, which is designed for drug assessment, should consider the societal, health and economic benefits of vaccines that offer future reductions in mortality/mobility.

Recommendation 8: Continue to evolve approval processes in line with international best practice with innovations such as adaptive licensing and a mechanism that provides assurances in downstream reimbursement approvals.

Recommendation 9: Where a medical product is known to be safe and effective outside of Australia, establish more efficient approval processes for importation and use in Australia, particularly when treating neglected or orphan diseases.

Submission made on behalf of the University of Melbourne

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